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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/931,375	08/17/2001	Matthew L. Warman	38464-0004	1602

24024 7590 10/26/2005

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CLEVELAND, OH 44114

EXAMINER

SEHARASEYON, JEGATHEESAN

ART UNIT PAPER NUMBER

1647

DATE MAILED: 10/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/931,375

Applicant(s)

WARMAN ET AL.

Examiner

Jegatheesan Seharaseyon, Ph.D

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 08 August 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 8,9,30 and 32-38 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 8,9,30 and 32-38 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

1. This office action is in response to the amendment and remarks filed on 8/8/04. Claim 31 has been cancelled. Claims 8, 9 and 30 are amended. Claims 37 and 38 have been newly added. Thus, claims 8, 9, 30 and 32-38 are pending.
2. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.
3. The Office also acknowledges the change in the specification.
4. The Office also acknowledges the changes to the Figures.

### ***Claim Objections***

5. Applicants amendments have necessitated the withdrawal of the objection to claim 8.
6. Claims 32 and 38 are objected to because it is dependent on cancelled claim. The Office is assuming that claim 32 is dependent on claim 30 and examined further. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

7. The rejection of claims 8,9 and 30 under 35 U.S.C 112, second paragraph, as being indefinite for failing to point out distinctly the subject matter is withdrawn because of Applicants amendments.
8. The rejection of claim 35 for lacking antecedent basis is maintained for reason stated in the Office Action dated 3/18/2005 (see page 5).

### ***Claim Rejections - 35 USC § 102***

9. Applicants amendments necessitated the withdrawal of the rejection of claims 8, 30 and 31 under 35 U.S.C 102(e) as being anticipated by Carulli et al.

***Claim Rejections - 35 USC § 103***

10. The pending rejections of claims 30-36 under 35 U.S.C 103(a) are withdrawn because of Applicants amendments. Applicants' arguments are moot because Applicants have modified the claims. Office notes that the receptor binding of various molecules is an inherent function of any receptor including the instant receptor (BSMR).

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action.

12. Claims 8, 9, 30, 32, 37 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carulli et al. (U. S. Patent NO. 6, 780, 609) and Dong et al. (1998, Ref B06 in PTO1449 of 10/15/02) in view of Tamai et al. (2000, Ref A24 in PTO1449 of 5/1/02).

The teachings of Carulli et al. have been discussed in the Office Action dated 3/18/2005 paragraph 9a and above in paragraph 10. The Zmax1 or HBM protein involved in the regulation of bone strength and mineralization disclosed by Carulli et al. (SEQ ID NO: 3) is different from SEQ ID NO: 2 of the instant invention at 3 positions possibly due to sequencing errors. Thus, the Office provides Dong et al., which is identical to SEQ ID NO: 2 (see Appendix A). This reference further teaches the mitogenic activity of this protein in osteoblastic cell line TE85 (see page 788). It is further suggested that this gene expression is regulated during osteoblast differentiation (see page 789). However, these references do not teach the modulation of this gene by WNT signaling. Tamai et al. (2000) describe that human LRP5 Human LRP5 and LRP6 share 71% amino-acid identity and together with Arrow, form a distinct subgroup of the LRP

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family. Arrow, LRP5 and LRP6 each contain an extracellular domain with a EGF (epidermal growth factor) repeats and LDLR repeats, followed by a transmembrane region and a cytoplasmic domain lacking recognizable catalytic motifs. Tamai et al. study the LRP5/LRP6 involvement in Wnt signaling by examining their function in Wnt-induced axis and neural crest formation in *Xenopus* embryos. It also teaches that although LRP5 alone did not induce axes, co-injecting LRP5 and Wnt-5a did induce axes (see page 531). Tamai et al. reference also discloses the induction LRP6 by Wnt-1 and Wnt-3a (see page 532).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use BSMR protein to modulate bone strength and mineralization as described by Carulli et al and Dong et al. using WNT proteins because Tamai et al. disclose that LRP5 is induced by WNT signaling. One of ordinary skill in the art would have been motivated to modulate BSMR (LRP5 or Zmax1 or LR3) using WNT signaling in order to regulate bone strength and mineralization. In addition, one of ordinary skill in the art would have been also been motivated because Tamai et al. describe the signal transduction of LRP5/LRP6 by Wnt (page 531). Therefore, the instant invention is *prima facie* obvious over Carulli et al. (U. S. Patent NO. 6, 780, 609) and Dong et al. (1998, Ref B06 in PTO1449 of 10/15/02) in view of Tamai et al. (2000, Ref A24 in PTO1449 of 5/1/02).

13. Claims 33 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carulli et al. (U. S. Patent NO. 6, 780, 609) and Dong et al. (1998, Ref B06 in PTO1449

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of 10/15/02) in view of Tamai et al. (2000, Ref A24 in PTO1449 of 5/1/02) and Oppermann et al. (U. S. Patent NO. 5, 652, 337).

The teachings of Carulli et al., Dong et al., Tamai et al. and Oppermann et al. have been described above and in the Office Action dated 3/18/2005, paragraph 10b (see page 9).

Specifically, Oppermann et al. disclose compounds that are capable of targeting BSMR effector to the region of bone remodeling (column 15, lines 38-42). For example, tetracycline and diphosphonates (bisphosphonates) are known to bind to bone mineral, particularly at zones of bone remodeling, when they are provided systemically in a mammal. Accordingly, these molecules may be included as useful agents for targeting OP-3 (a morphogen) to bone tissue. Alternatively, an antibody or other binding protein that interacts specifically with a surface molecule on the desired target tissue cells also may be used (column 15, lines 38-47).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to target BSMR effector molecules to regions of bone regeneration or remodeling to modulate bone strength and mineralization as described by Carulli et al., Dong et al. and Tamai et al. collectively using tetracycline and diphosphonates (bisphosphonates) that are known to bind to bone mineral because Oppermann et al. disclose that tetracycline and diphosphonates (bisphosphonates) are known to bind to bone mineral, particularly at zones of bone remodeling, when they are provided systemically in a mammal. One of ordinary skill in the art would have been motivated to modulate BSMR (LRP5 or Zmax1 or LR3) using a BSMR effector such as Wnt that is

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targeted to bone producing or remodeling region by compounds such as tetracycline and diphosphonates (bisphosphonates) in order to regulate bone strength and mineralization to treat osteoporosis. Therefore, the instant invention is *prima facie* obvious over Carulli et al. (U. S. Patent NO. 6, 780, 609) and Dong et al. (1998, Ref B06 in PTO1449 of 10/15/02) in view of Tamai et al. (2000, Ref A24 in PTO1449 of 5/1/02) and Oppermann et al. (U. S. Patent NO. 5, 652, 337).

14. Claims 35 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carulli et al. (U. S. Patent NO. 6, 780, 609) and Dong et al. (1998, Ref B06 in PTO1449 of 10/15/02) in view of Tamai et al. (2000, Ref A24 in PTO1449 of 5/1/02) further in view of Wang et al. (U. S. Patent NO. 6, 245, 889) and Hughes et al (1995).

The teachings of Carulli et al., Dong et al., Tamai et al., Wang et al. and Hughes et al. have been described above and in the Office Action dated 3/18/2005, paragraph 10c (see page 10).

Wang et al. disclose the use of BMP-2 and BMP-4 protein may be combined with other agents beneficial to the treatment of the bone and/or cartilage defect, wound, or tissue in question (column 6, lines 65 to column 7, lines 42). These agents include various growth factors such as epidermal growth factor (EGF), platelet derived growth factor (PDGF), transforming growth factors (TGF- $\alpha$  and TGF- $\beta$ ), and insulin-like growth factor (IGF) (column 7, lines 2-5). In addition, these agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone forming cells (column 6, lines 20-23). Wang et al. also teach that for bone and/or cartilage formation, the composition would include a

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matrix capable of delivering BMP-2, BMP-4 or other BMP proteins to the site of bone and/or cartilage damage (column 7, lines 35-38). It also teaches that BMP-2 may be used individually in a pharmaceutical composition or in combination with BMP-4 and/or one or more of the other BMP proteins (column 7, lines 14-18). Hughes et al. (1995) disclose that the effect of BMPs on nodule formation was seen after only 24 hours of exposure to BMPs. It also teaches that continuous or 24-h exposure to BMP-2 or BMP-4 increased the number of postmitotic ALP-positive cells in log phase culture (abstract). Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer another bone morphogenic protein (BMP) target to regions of bone regeneration or remodeling to modulate bone strength and mineralization as described by Wang et al. using a bone morphogenic protein such as BMP-2 administering BMP-2 at least 24 hrs prior administering the BSMR effector as taught by Hughes et al to increase bone formation because Carulli et al., Dong et al. and Tamai et al. collectively disclose that by manipulating the levels of functional Zmax1 or LRP5 or LR3 protein, it is possible to affect bone development and to increase or decrease levels of bone mineralization, particularly at zones of bone remodeling, when they are provided systemically in a mammal. One of ordinary skill in the art would have been motivated to treat osteoporosis by administering BMP-2 protein 24 hrs prior to providing BSMR effector that is targeted to bone producing or remodeling region in order to regulate bone strength and mineralization to treat osteoporosis. Further, Hughes teaches that BMP-2 or BMP-4 increased the number of postmitotic ALP-positive cells. Therefore, the instant invention is *prima facie* obvious over Carulli et al.



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(U. S. Patent NO. 6, 780, 609) and Dong et al. (1998, Ref B06 in PTO1449 of 10/15/02) in view of Tamai et al. (2000, Ref A24 in PTO1449 of 5/1/02) and Oppermann et al. (U. S. Patent NO. 5, 652, 337).

15. No Claims are allowable.

Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

#### ***Contact Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon, Ph.D whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-

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273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JSS 10/05

  
JANET L. ANDRES  
SUPERVISORY PATENT EXAMINER

Applicants copy

Appendix A1

GenCore version 5.1.6  
Copyright (c) 1993 - 2005 Compugen Ltd.

OM protein - protein search, using sw model

Run on: February 17, 2005, 01:16:38 / Search time 224 Seconds

(without alignments)  
3691.999 Million cell updates/sec

Title: US-09-931-375A-2

Sequence: 1 MEAAPGPPWPLLLLLLL.....TERSYFLPPPPSPCTDS 1615

Scoring table: BLOSUM62  
Gapop 10.0, Gapext 0.5

Searched: 1612378 seqs, 512079187 residues

Total number of hits satisfying chosen parameters: 1612378

Minimum DB seq length: 0  
Maximum DB seq length: 200000000

Post-processing: Minimum Match 0  
Maximum Match 100  
Listing first 45 summaries

Database: UniProt\_03:  
1: uniprot\_sprot:  
2: uniprot\_trembl:

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

## SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	8740	100.0	1615	09US7	Q9US77 homo sapien
2	8736	100.0	1615	LRP5_HUMAN	Q9US77 homo sapien
3	8259.5	94.5	1614	LRP5_MOUSE	Q9US77 mus musculu
4	7132.5	81.6	1605	Q8AYF1	Q8AYF1 xenopus lae
5	6133.5	70.4	1613	LRP6_HUMAN	Q8AYF1 homo sapien
6	6097.5	69.8	1613	LRP6_MOUSE	Q8AYF1 mus musculu
7	6084	69.6	1613	Q8AYF0	Q8AYF0 xenopus lae
8	3537.5	40.4	1678	Q9SV09	Q9SV09 drosophila
9	3536.5	40.3	1678	Q9V6Q0	Q9V6Q0 drosophila
10	3521.5	40.3	1678	Q9V6Q0	Q9V6Q0 drosophila
11	3262.5	37.3	1698	Q7PV65	Q7PV65 anopheles g
12	2788	31.9	1246	Q6AWJ8	Q6AWJ8 drosophila
13	2687	30.7	1905	LRP4_RAT	Q9GYP1 rattus norv
14	2687	30.7	1905	Q76LU2	Q76LU2 rattus norv
15	2686	30.7	1905	LRP4_HUMAN	Q8Y156 homo sapien
16	2671	30.6	1905	LRP4_MOUSE	Q8Y156 mus musculu
17	2654	30.4	1721	Q7V501	Q7V501 oryctolagus
18	2266.5	25.9	1768	Q7V501	Q7V501 oryctolagus
19	2228	25.5	2009	Q9V6M0	Q9V6M0 anopheles g
20	2193	25.1	4544	LRP1_HUMAN	Q9US77 homo sapien
21	2180	24.9	4543	LRP1_MOUSE	Q9US77 mus musculu
22	2165	24.8	4545	Q912X7	Q912X7 mus musculu
23	2165	24.8	4545	Q920Y4	Q920Y4 mus musculu
24	2113	24.2	4545	Q61291	Q61291 mus musculu
25	2018	23.1	1721	Q8WY30	Q8WY30 homo sapien
26	2008	23.0	4539	LRP1_HUMAN	Q9US77 homo sapien
27	1997	22.8	4539	LRP1_MOUSE	Q9US77 mus musculu
28	1876.5	21.5	4655	LRP2_HUMAN	Q9US77 homo sapien
29	1876.5	21.5	4655	Q725C0	Q725C0 homo sapien
30	1872.5	21.4	4655	Q725C1	Q725C1 homo sapien
31	1856	21.2	4660	LRP2_RAT	Q9US77 rattus norv

32	1779.5	20.4	4569	Q7P335	Q7P335 anopheles g
33	1762.5	20.2	4699	Q9V383	Q9V383 drosophila
34	1759.5	20.1	4547	Q9W343	Q9W343 drosophila
35	1708	19.5	4569	Q7PV66	Q7PV66 anopheles g
36	1458	16.7	4753	LRP_CAEEL	Q04833 caenorhabdi
37	1044.5	12.0	1581	Q73809	Q73809 fugu rubrip
38	1024	11.7	252	Q9NSY4	Q9NSY4 homo sapien
39	980.5	11.2	1859	Q7PS28	Q7PS28 anopheles g
40	969	11.1	1809	Q8MP02	Q8MP02 periplaneta
41	914.5	10.5	1847	Q76952	Q76952 bedes segyp
42	909.5	10.4	1984	YL_DROME	Q9US77 drosophila
43	902.5	10.3	1650	Q9QV76	Q9QV76 rattus sp.
44	876.5	10.0	881	Q8WY31	Q8WY31 homo sapien
45	859	9.8	1537	Q8WY29	Q8WY29 homo sapien

## ALIGNMENTS

## RESULT 1

ID Q9US77 PRELIMINARY; PRT; 1615 AA.

AC Q9US77;  
DT 01-MAY-2000 (TRMBLrel. 13, Created)  
DT 01-MAY-2000 (TRMBLrel. 13, Last sequence update)  
DT 01-JUN-2003 (TRMBLrel. 24, Last annotation update)  
DS LDL receptor member LR3.  
OS Homo sapiens (Human).  
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;  
OC Mammalia; Eutheria; Primates; Catarrhini; Homiidae; Homo.  
OX NCBI\_Taxid-9606;  
RN [1]  
RP SOURCE: FROM N.A.  
RX MEDLINE:99008902; PubMed-9790987; DOI-10.1006/birc.1998.9545;  
RA Dong Y., Lathrop W., Weaver D., Qiu Q., Cini J., Bertolini D.,  
RA Chen D.;  
RT "Molecular cloning and characterization of LR3, a novel LDL receptor  
RT family protein with mitogenic activity.";  
RL Biochem. Biophys. Res. Commun. 251:784-790(1998).  
DR EMBL; AF077820; AAC72791.1; -  
DR HSSP; P98162; LRP.  
DR GO; GO:0016020; C:membrane; IRA.  
DR GO; GO:0004872; F:receptor activity; IRA.  
DR InterPro; IPR006209; BGF-like.  
DR InterPro; IPR006210; BGF.  
DR InterPro; IPR002172; LDL\_receptor\_A.  
DR InterPro; IPR000033; LDL\_receptor\_rep.  
DR Pfam; PF00008; BGF; 3.  
DR Pfam; PF00057; LDL\_recept\_d; 3.  
DR Pfam; PF00058; LDL\_recept\_a; 3.  
DR PRINTS; PR00261; LDLRECEPTOR.  
DR SMART; SM00181; BGF; 4.  
DR SMART; SM00192; LDLA; 3.  
DR SMART; SM00135; LY; 20.  
DR PROSITE; PS01209; LDLRA\_1; 3.  
DR PROSITE; PS00068; LDLRA\_2; 3.  
KW Receptor.  
SQ SEQUENCE 1615 AA; 179143 MW; 8BA25D07F51B02CA CRC64;

## Query Match

Best Local Similarity 100.0%; Pred. No. 0;  
Matches 1615; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY	1	MEAAPGPPWPLLLLLLLALGCPAPAPASPLLPANRRDRLVADAGVQLSESTIVS	60
DB	1	MEAAPGPPWPLLLLLLLALGCPAPAPASPLLPANRRDRLVADAGVQLSESTIVS	60
QY	61	GLEDAAVDFQSGAVYWTDSBAIKQTYLNTGAAVONTVISGLVSPDGLACMVGK	120
DB	61	GLEDAAVDFQSGAVYWTDSBAIKQTYLNTGAAVONTVISGLVSPDGLACMVGK	120
QY	121	KLYWDSRTNIRIVANNGTSRKVLFWQDDOPRAIALDAHQYWTWTGQETPRIRAG	180
DB	121	KLYWDSRTNIRIVANNGTSRKVLFWQDDOPRAIALDAHQYWTWTGQETPRIRAG	180

Applicant's copy

Applicant's Appendix A 2

Db 121 KLYTDSSTNRLEVNANLCTSRKVLPMQDLPAPALADPAHGYMTWNGETPRJERQ 180  
 Qy 181 MDGSTRKIIIVSDIYWPNGLTIDLEBQCLYANADKSPPIRANLDGSPROKVEGSLTTP 240  
 Db 181 MDGSTRKIIIVSDIYWPNGLTIDLEBQCLYANADKSPPIRANLDGSPROKVEGSLTTP 240  
 Qy 241 FULTLSGDPLVMTDMQTSIHAQNRRTGGRKELLSALYSPNDIYQLSGRQPFPTTRCE 300  
 Db 241 FULTLSGDPLVMTDMQTSIHAQNRRTGGRKELLSALYSPNDIYQLSGRQPFPTTRCE 300  
 Qy 301 EDNGGCSHLCLSPSPPTTCACPTGVQVQDNNGTCCAGAEVLLAERTDLARIISLDP 360  
 Db 301 EDNGGCSHLCLSPSPPTTCACPTGVQVQDNNGTCCAGAEVLLAERTDLARIISLDP 360  
 Qy 361 DPTDIYQVDDIRHAIADYDPLSGYVMTDEBRARIRAYLDGSAQTLVMTLENDPG 420  
 Db 361 DPTDIYQVDDIRHAIADYDPLSGYVMTDEBRARIRAYLDGSAQTLVMTLENDPG 420  
 Qy 421 IADVVAARLVMTDGTDRIRIVTLNGTSRKILVSEDLDEPRAIYALHPVGLMTWDMGE 480  
 Db 421 IADVVAARLVMTDGTDRIRIVTLNGTSRKILVSEDLDEPRAIYALHPVGLMTWDMGE 480  
 Qy 481 NPKRICANLDGGERAVLVNALSIGMPNGIALDQSGKLYMGDAITDRIYVNDGTERTL 540  
 Db 481 NPKRICANLDGGERAVLVNALSIGMPNGIALDQSGKLYMGDAITDRIYVNDGTERTL 540  
 Qy 541 LEDKLPRIIPGTLTADPTIYMTDMQSRISIRVHVKSRLVYIDQLDMLGKAVVAVKV 600  
 Db 541 LEDKLPRIIPGTLTADPTIYMTDMQSRISIRVHVKSRLVYIDQLDMLGKAVVAVKV 600  
 Qy 601 GTPNCADNRNGGCSHLCPFTPHATRCQGPIGLELSDMKCTIVEALVTSRAAIIHRI 660  
 Db 601 GTPNCADNRNGGCSHLCPFTPHATRCQGPIGLELSDMKCTIVEALVTSRAAIIHRI 660  
 Qy 661 ETRNNDAVAPLVTVGEASALDPDVSNHIIYTWDSLKTISRANPSSVEHVEFGOLDYP 720  
 Db 661 ETRNNDAVAPLVTVGEASALDPDVSNHIIYTWDSLKTISRANPSSVEHVEFGOLDYP 720  
 Qy 721 EGNADVMMGKLVYADTCTNRLEVARLDGQPROVLYWRDLNDRSLALDPTGYTYMTEM 780  
 Db 721 EGNADVMMGKLVYADTCTNRLEVARLDGQPROVLYWRDLNDRSLALDPTGYTYMTEM 780  
 Qy 781 GCKPPIVAAVMDGTCNCTLVNKGVRANDLTIDYADQRLTWTDLITNMISSNLQGERV 840  
 Db 781 GCKPPIVAAVMDGTCNCTLVNKGVRANDLTIDYADQRLTWTDLITNMISSNLQGERV 840  
 Qy 841 IADDLPHFPGLTQYSDVYIYTDWNLHSGIERADKTSGRNRTLQSHLDFWMDLVTHSSRQ 900  
 Db 841 IADDLPHFPGLTQYSDVYIYTDWNLHSGIERADKTSGRNRTLQSHLDFWMDLVTHSSRQ 900  
 Qy 901 DGLANCCANNQCCQCLAIIPGGRCCASHYTLDPSSNRCSPPTTLLFSQKASISRI 960  
 Db 901 DGLANCCANNQCCQCLAIIPGGRCCASHYTLDPSSNRCSPPTTLLFSQKASISRI 960  
 Qy 961 PDDGHSPLILPLHGLANVAYADYDPLDKETIYVWDGRONIKAKODGTQPFVLTSLSQO 1020  
 Db 961 PDDGHSPLILPLHGLANVAYADYDPLDKETIYVWDGRONIKAKODGTQPFVLTSLSQO 1020  
 Qy 1021 NPDRPHDLSTIDISRTLPFTCEATNTINVHLSGEMGVYLRGDRKPRATVVAERGY 1080  
 Db 1021 NPDRPHDLSTIDISRTLPFTCEATNTINVHLSGEMGVYLRGDRKPRATVVAERGY 1080  
 Qy 1081 LYFTNMODRAKIERAALDGTREBEVLTGILIPVALVVDNTLGLFVWVADLKRISCD 1140  
 Db 1081 LYFTNMODRAKIERAALDGTREBEVLTGILIPVALVVDNTLGLFVWVADLKRISCD 1140  
 Qy 1141 LSGANRLTLEDPANVOPLGLITLIGKLVYTDROQOQIEVEKCTGDKTRIQGVYAHITG 1200  
 Db 1141 LSGANRLTLEDPANVOPLGLITLIGKLVYTDROQOQIEVEKCTGDKTRIQGVYAHITG 1200  
 Qy 1201 IHAVERVSLERFSANPCARDNGGCSHICAKGDGTGRCSVHLVILQNLITCSEPTCS 1260  
 Db 1201 IHAVERVSLERFSANPCARDNGGCSHICAKGDGTGRCSVHLVILQNLITCSEPTCS 1260

Qy 1261 PDGFACATGEIDICIRKAWRCDGFPECDDQSDDEGCPVCSAAGPCARGQCVDLRLRCDE 1320  
 Db 1261 PDGFACATGEIDICIRKAWRCDGFPECDDQSDDEGCPVCSAAGPCARGQCVDLRLRCDE 1320  
 Qy 1321 ADCQDSDEADGDAICLPRNRCASGQCVLTKQCCSDPPDICSDHLMCEITKPSDDG 1380  
 Db 1321 ADCQDSDEADGDAICLPRNRCASGQCVLTKQCCSDPPDICSDHLMCEITKPSDDG 1380  
 Qy 1381 PAHSAIGVIGIILSLFVGGVYVCCORVVCORVAGANPPEHRYSGTPHPLNFIAP 1440  
 Db 1381 PAHSAIGVIGIILSLFVGGVYVCCORVVCORVAGANPPEHRYSGTPHPLNFIAP 1440  
 Qy 1441 GSGQGPFTGLICGSMSSSVSLMGGRGVPLVYRNAYTQASSSSSTKATLYPPIIAP 1500  
 Db 1441 GSGQGPFTGLICGSMSSSVSLMGGRGVPLVYRNAYTQASSSSSTKATLYPPIIAP 1500  
 Qy 1501 PPSPATDPELYNMDPFYSNIPATAPRYPIYIRGMAPPTTGSTVDCOSDYSASRMKAS 1560  
 Db 1501 PPSPATDPELYNMDPFYSNIPATAPRYPIYIRGMAPPTTGSTVDCOSDYSASRMKAS 1560  
 Qy 1561 KYTLIDNSDSPPPPPPPHSOYLASBDCSPSPATERSYFHLPPPPSPCTDSS 1615  
 Db 1561 KYTLIDNSDSPPPPPPPHSOYLASBDCSPSPATERSYFHLPPPPSPCTDSS 1615

RESULT 2  
 LRP5 HUMAN  
 ID LRP5\_HUMAN STANDARD: PRT: 1615 AA.  
 AC 075157; OS6P26; OSUP66;  
 DT 05-JUL-2004 (Rel. 44, Created)  
 DT 05-JUL-2004 (Rel. 44, Last sequence update)  
 DT 25-OCT-2004 (Rel. 45, Last annotation update)  
 DE Low-density lipoprotein receptor-related protein 5 precursor.  
 GN Name=LRP5; Synonym=LRP7;  
 OS Homo sapiens (Human).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Primates; Catarrhini; Homnidae; Homo.  
 OC NCBI\_Taxid=9606;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RC TISSUE=osteoblast;  
 RX MEDLINE=98382578; PubMed=9714764; DOI=10.1016/S0378-1119(98)00311-4;  
 RA Hey P.J., Twells R.C.J., Phillips M.S., Nakagawa Y., Brown S.D.,  
 RA Kawaguchi Y., Cox R., Xie G., Dugan V., Hammond H., Metzker M.L.,  
 RA Todd J.A., Hest J.F.;  
 RT Cloning of a novel member of the low-density lipoprotein receptor  
 RT family.  
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 RN [2]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=2195044; PubMed=11401438; DOI=10.1006/geno.2000.6492;  
 RA Twells R.C.J., Metzker M.L., Brown S.D., Cox R., Garey C., Hammond H.,  
 RA Hey P.J., Levy E., Nakagawa Y., Phillips M.S., Todd J.A., Hest J.F.;  
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 RT Genomics 72:231-242(2001).  
 RN [3]  
 RP SEQUENCE FROM N.A.  
 RX PubMed=12509515; DOI=10.1073/pnas.0133792100;  
 RA Fujino T., Asaba H., Kang M.J., Ikeda Y., Sone H., Takada S.,  
 RA Kim D.H., Ioka R.X., Ong M., Tomoyori H., Okubo M., Murase T.,  
 RA Kametaki A., Yamamoto J., Magoori K., Takahashi S., Miyamoto Y.,  
 RA Oishi H., Nose M., Okazaki M., Usui S., Imatsumi K., Yanagisawa M.,  
 RA Sakai J., Yamamoto T.T.;  
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 RT insulin secretion.  
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 RX PubMed=1471402; DOI=10.1016/S1097-2765(03)00484-2;  
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